REVIEW

Is asthma over- or under-diagnosed in athletes?

J.-B. LANGDEAU AND L.-P. BOULET

Institut Universitaire de cardiologie et de pneumologie de l'Université Laval, Hôpital Laval, Québec, Canada

Abstract A high prevalence of asthma has been reported in athletes. However, studies in this population usually show an even higher prevalence of airway hyperresponsiveness (AHR) and exercise-induced bronchoconstriction (EIB). This report compares studies on self-reported or physician-diagnosed asthma in athletes with those using objective measures of airflow limitation or airway responsiveness. The higher prevalence of AHR (or EIB) measured in athletes, when compared with the prevalence of self-reported or physician-diagnosed asthma, suggests that abnormal airway responses are common in athletes, although they are infrequently associated with troublesome respiratory symptoms. This may indicate underdiagnosis of asthma in athletes, possibly due to an underreporting of respiratory symptoms or a reduction in perception of nociceptive sensations with repeated exercise over time, or it may simply mean that high-level training is associated with asymptomatic AHR. In athletes, as in the general population, the use of subjective methods such as surveys and questionnaires results in an underestimation of the prevalence of airway dysfunction when compared with objective measurements. The significance of these observations is unknown, and there is a need to determine their long-term consequences for athletes.

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Keywords athletes; asthma; airway hyperresponsiveness; exercise-induced bronchoconstriction; perception of bronchoconstriction.

INTRODUCTION

A growing body of evidence suggests that high-intensity exercise, done on a regular basis, could contribute to the development of asthma and/or airway hyperresponsiveness (AHR) in athletes (1,2) However, in the studies reporting a high prevalence of AHR or airflow obstruction in athletes, we observed a general discrepancy between the number subjects with a diagnosis of asthma and those showing a significant fall in forced expiratory volume in one second (FEV_1) after exercise, or a positive histamine or methacholine challenge test (2–6). Indeed, the prevalence of self-reported or physician-diagnosed asthma in athletes is usually much lower than that of AHR or exercise-induced asthma/bronchoconstriction (EIA/EIB) (2,17–24). This phenomenon may also be observed in the general population (25), but appear more accentuated in athletes.

In this report, we reviewed these observations and compare the published findings on the prevalence of self-reported or physician-diagnosed asthma with the ones of AHR or EIB in athletes. This was done through a search of the National Library of Medicine database "Pub Med" using the following keywords: athletes, prevalence, exercise-induced asthma or bronchoconstriction, airway or bronchial hyperresponsiveness and asthma. No limited time frame was applied. We only analyzed the publications written in English who where assessing the prevalence of asthma or airway response to various stimuli among athletes. Publications with insufficient description of the methodology or unclear data were excluded. We also excluded studies with a total number of subjects less than 25. Finally, we discuss the possible causes and implications of these observations.

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Correspondence should be addressed to: Dr Louis-Philippe Boulet, Hôpital Laval, 2725, Chemin Sainte-Foy, Sainte-Foy, Québec, Canada GIV 4G5. Fax: +1 418 656 4762; E-mail: lpboulet@med.ulaval.ca

EVALUATION OF ATHLETES' PULMONARY FUNCTION

In athletes, as in the general publication, respiratory problems can be evaluated by various methods. Questionnaires and surveys are among the most widely used. They make it possible to study a large number of individuals and avoid the task of recruiting subjects for laboratory testing; they also require less time commitment

from busy athletes and are inexpensive. However, the data collected by these methods may not always accurately reflect the respiratory condition of the participating athletes. Indeed, self-reported asthma, physician-diagnosed asthma and respiratory symptoms, all of which are frequently recorded in surveys and questionnaires, have the disadvantage of relying on subjective perception.

Among the objective methods for evaluating the respiratory condition of athletes, the most common is the change in FEV_1 before and after exercise. A criterion of $\geq$10% or 15% fall in FEV_1 after exercise is often proposed as a measure of EIB. Although EIB is often equated with asthma in athletes, it mostly identifies a physiological response to exercise and may not always correlate well with bronchial response to other triggers or with respiratory symptoms (26). Methacholine or histamine challenge tests are also used to determine the degree of AHR in athletes. Although these objective methods are more demanding than questionnaire-based surveys, they are well standardized and evaluate more effectively the type and magnitude of airway response.

SUBJECTIVE VS. OBJECTIVE MEASURES OF ABNORMAL AIRWAY RESPONSES IN ATHLETES

Table I illustrates studies on the prevalence of asthma reported from survey questionnaires, and Table 2, the prevalence of AHR or EIB obtained from objective testing. The criteria used to determine the prevalences of asthma were based either on individual self-reporting of asthma or a diagnosis of asthma previously made by a physician. When comparing those reported prevalences of asthma with the measured prevalences of AHR/EIB found in studies reported in Table 2, one notes a general discrepancy. Objective measures of AHR were made (at rest) either with methacholine or histamine bronchoprovocation. A 15 or 20% fall in FEV_1 at specific provocation dose (PD_{15} or PD_{20}) or provocation concentration (PC_{20}) of methacholine or histamine were used to make the diagnosis of AHR, as showed in Table 2. The diagnosis of EIB was determined from the percentage fall (10, 15 or 20%) in expiratory flows such as FEV_1 or peak expiratory flow (PEF) after exercise.

In Table I, although there are variations between the listed prevalences of self-reported or physician-diagnosed asthma in athletes, these prevalences rarely exceeds the level of 20% of the population studied (2,17–24). As shown in Table 2, however, the prevalences of AHR or EIB obtained from objective measurements for the various study groups are much higher than that obtained from non-objective means; generally above the level of 20% (2–16). This trend is not exclusive to the athlete population; in the studies (Tables I and 2) including control subjects (either non-athlete or sedentary subjects) paired for age with the athlete group, this tendency was also observed.

Although the identification of a $\geq$10% fall in FEV_1 is believed to be more sensitive for detection of EIB (Table 2), studies using this criterion did not always find a greater prevalence than studies using the criterion of $\geq$15% or $\geq$20% fall in FEV_1. Furthermore, studies measuring the prevalence of AHR with the criterion of a 20% fall in

Table I. Self-reported or physician-diagnosed asthma from questionnaire

Authors (ref.)	Year	Criteria for asthma	Sport (% prevalence)	No. athletes/controls
Langdeau *et al.* (2)	2000	Self-reported or physician-diagnosed	LDR+MB (20)*, SWI (8), CCS+SKA (28)*, TRI (8), C (4)	100/50
Weiler and Ryan (17)	2000	Physician-diagnosed	WOA (22), C (−)	196
Nystad *et al.* (18)	2000	Self-reported	MIS (10), C (7)	1620/1680
Weiler *et al.* (19)	1998	Physician-diagnosed	SOA (15), C (−)	699
Helenius *et al.* (20)	1997	Physician-diagnosed	LDR (17)*, SP (8), C (3)	213/124
Kujala *et al.* (21)	1996	Physician-diagnosed	MIS (2), C (4)	1282/777
Hier and Oseid (22)	1994	Physician-diagnosed	CCS (14)*, C (5)	153/306
Voy (23)	1986	Physician-diagnosed	SOA (11)[a], C (−)	597
Fitch (24)	1984	Physician-diagnosed	SOA (9), C (−)	291

Figures in parentheses have been rounded (0–0.4 = 0 and 0.5–0.9 = 1) to eliminate decimals and represent the percentage prevalence of self-reported or physician-diagnosed asthma reported by authors, from self-administrated questionnaire method.

No, number of subjects; C(−), No control subjects enrolled in the study.

BAS, basketball; CCS, cross-country skiing; FOT, football, HOC, hockey; HSS, High-school students; LDR, long-distance running; MB, mountain-biking; MIS, miscellaneous athletes; SKA, skating; SOA, Summer Olympic athletes; SP, speed and power; SWI, swimming; T & F, track and field; TRI; triathlon; WOA, Winter Olympic athletes and C; control group.

[a]Percentage of subjects with EIA and/or asthma.

Table 2. Prevalence of AHR or EIB from objective measurements

Authors (ref.)	Year	Method	Sport (% prevalence)	No. athletes/controls
Langdeau *et al.* (2)	2000	Methacholine $PC_{20} \leq 16$ mg/ml	LDR+MB (32), CCS+SKA (52)* TRI (32), SWI (76)*, C (28)	100/50
Wilber *et al.* (3)	2000	$\geq$ 10% fall FEV_1	WOA (23), C (−)	170
Mannix *et al.* (4)	1999	$\geq$ 10% fall FEV_1[a]	SKA (31), C (−)	29
Leuppi *et al.* (5)	1999	Methacholine $PD_{20} \leq 2$ mg/ml	BAS (21), HOC (35)*, C (−)	50
Helenius *et al.* (6)	1998	Histamine $PD_{15} \leq 1.6$ mg/ml	SP (18), LDR (9), SWI (36)*, C (11)	162/45
Helenius *et al.* (7)	1998	Histamine $PD_{15} \leq 1.6$ mg/ml	SWI (48)*, C (16)	29/19
Schoene *et al.* (8)	1997	$\geq$ 10% fall FEV_1	TF (15)[b], C (−)	189
Potts *et al.* (9)	1996	Methacholine $PC_{20} \leq 16$ mg/ml	SWI (60)*, C (13)	35/16
Mannix *et al.* (10)	1996	$\geq$ 10% fall FEV_1	SKA (35), C (−)	124
Provost-Craig *et al.* (11)	1996	$\geq$ 10% fall FEV_1 or FEF_{25-75}	SKA (30), C (−)	100
Sue-Chu *et al.* (12)	1996	Methacholine $PD_{20} \leq 1800$ μg	CCS (23)[b], C (−)	171
Feinstein *et al.* (13)	1996	$\geq$ 15% fall FEV_1	FOT (19), C (−)	48
Feinstein *et al.* (13)	1996	$\geq$ 15% fall PEF	FOT (35), C (−)	48
Brudno *et al.* (14)	1994	$\geq$ 10% fall FEV_1	HSS (47), C (−)	397
Brudno *et al.* (14)	1994	$\geq$ 15% fall FEV_1	HSS (31), C (−)	397
Brudno *et al.* (14)	1994	$\geq$ 20% fall FEV_1	HSS (23), C (−)	397
Pierson and Voy (15)	1988	$\geq$ 10% fall PEF	SOA (14)[b], C (−)	597
Weiler *et al.* (16)	1986	Methacholine $PD_{20} \leq 25$ mg/ml	FOT (50), BAS (25), C (41)	167/167

Figures in parentheses have been rounded (0–0.4=0 and 0.5–0.9= 1) to eliminate decimals and represent the percentage prevalence of AHR or EIB reported by authors.

No, number of subjects; C(−), no control subjects used in the study.

Methacholine; methacholine challenge test; histamine; histamine challenge test; FEV_1; forced expiratory volume in 1 s; PEF; peak expiratory flow; FEF_{25-75}; Forced expiratory flow at 25 and 75% of the vital capacity for other abbreviations, refer to Table 1.

*Value significantly different ($P < 0.05$) from the control group.

[a]Prevalence of subjects presenting with at least one of the following test: $\geq$10% fall in FEVI, or $\geq$25% fall in PEF, or $\geq$20 fall in maximum mid-expiratory flow.

[b]Prevalence generated from analysis of authors data.

FEV_1 at various cutoff concentrations of methacholine or histamine, reported a percent prevalence of AHR relatively similar to those based on the fall in FEV_1 after exercise. Interestingly, of all sports disciplines presented in Table 2, swimming shows the highest prevalence of AHR to agonists such as methacholine or histamine, ranging from 36 to 76%.

The discrepancy between subjective and objective assessments of airway dysfunction, however, seems less marked among Olympians than other categories of athletes. In studies conducted on Summer Games Olympic athletes, Fitch (24), Voy (23) and Weiler and Ryan (19) obtained prevalences of 9.3, 11.2 and 15.3%, respectively, for the diagnosis of asthma, while Pierson and Voy (15) obtained a 14.2% prevalence from objective measures of EIB. The same trend can be observed in two recent studies on Winter Games Olympic athletes (3,17). Weiler and Ryan reported that 21.9% of these athletes had a diagnosis of asthma, while Wilber *et al.* identified EIB in 23% of them. There is no obvious explanation for this lack of discrepancy between the prevalences from subjective and objective assessments among the studies done on Olympic level athletes. Perhaps, the studies done by Wilber *et al*. (3) and Pierson and Voy (15) (Table 2) would have yielded higher prevalences if AHR to methacholine or histamine had been measured instead of EIB. The similarity between the prevalence of physician-diagnosed asthma reported by Weiler and Ryan (17) and the prevalence of EIB reported by Wilber *et al.* (3) could indicate that Winter Olympic athletes are more closely followed for detection of asthma than other athletes or that they more accurately perceived their respiratory symptoms. Another explanation could be that athletes with bothersome respiratory problems are less likely to advance to the elite level.

To our knowledge, only one study has reported a lower prevalence of diagnosis of asthma in athletes compared with controls (21). Kujala did a retrospective study on former male athletes who took part in at least one international competition between 1920 and 1965. Among the 1282 athletes who were still alive in 1985, 30 (2.4%) mentioned having a history of diagnosed asthma during the period up to 1985, compared with 27/777 (3.5%) control subjects. These findings could imply that the prevalence of asthma increased over the decades leading up to 1985, that underrecognition of respiratory disease was more common among these athletes, or that asthma and AHR either are transient or become clinically silent over time in athletes.

SUBJECTIVE VS. OBJECTIVE MEASURES OF ABNORMAL AIRWAY RESPONSES IN THE NORMAL POPULATION

A discrepancy between respiratory symptoms and pulmonary function tests has been frequently documented (27,28). It may therefore not be surprising that a difference between the prevalence of physician-diagnosed asthma and objective assessment of AHR has also been observed in the general population. Chowgule *et al*. investigated the population of Bombay and found a 3.5% prevalence of physician-diagnosed asthma, while the prevalence of AHR was 17%, with the criteria of a 20% fall in FEV_1 with $\leq$2.0 mg/ml of methacholine (25). Other investigators have reported a prevalence of physician-diagnosed asthma among the general population of 4.5%–7.2% (29–31).

When we look at the prevalence of AHR, for athletes as for the general population, objective assessment methods are more efficient than subjective ones at detecting changes in airway function. Manfreda *et al*. evaluated adults of the general population in six large Canadian cities and found that the prevalence of AHR to methacholine ranged from 13 to 29% (32). Also, studies of Trigg *et al*. and Renwick and Connolly reported a prevalence of AHR to methacholine of 23 and 34%, respectively (33,34).

HOW CAN WE EXPLAIN THE VARIATION IN PREVALENCE OF AIRWAY DYSFUNCTION IN ATHLETES?

The discrepancy observed between objective and subjective tests may be the result of various factors, as shown in Table 3.

Is increased airway response the normal results of supraphysiologic stimulus?

The increased prevalence of heightened airway responses to inhaled constrictor agent observed in athletes may not only suggest the presence of an abnormal condition such as asthma, but could be the reflection of a normal response to a supraphysiologic stimulus such as high-intensity exercise. EIB, however, does not seem to result only from such "normal" response to a "supranormal" stimulus, as it has been shown that airways were also abnormally responsive to non-physical stimuli such as methacholine or histamine. It is possible, as previously suggested by Anderson in a thorough review of exercise-induced asthma, that the humidifying process taking place in the small airways, in response to exercise, could lead to airway edema and/or mucus secretion and that in combination with the "physiological" shortening of smooth muscles would amplify the airway narrowing with a resulting reduction in FEV_1 (35).

Table 3. Possible causes of the discrepancy between physician-diagnosed asthma and airway hyperresponsiveness in athletes

(1) AHR as an transient and reversible result of a supraphysiologic stimulus (intense prolonged exercise)?
(2) Presence of asymptomatic AHR (no translation of AHR to respiratory symptoms)?
Minimal variation of airflow obstruction?
Insufficient airway inflammation?
Site of airway changes (small vs large airways)?
(3) Under-diagnosis of asthma in athletes?
Poor perception of respiratory symptoms?
Under-report of symptoms by athletes (interpreted as "normal")?
Temporal adaptation to nociceptive stimuli?
Under- diagnosis by physicians (misinterpretation of symptoms, no objective measures)?

Is high-intensity exercise a cause of asymptomatic airway hyperresponsiveness?

The role of the epithelium in the development of asthma and AHR has been demonstrated extensively (36). Airway epithelium is under major stress during high-intensity exercise. In dogs, it has been shown that repeated hyperventilation could induce AHR, but also peripheral airway inflammation, obstruction, and impaired beta-agonist-induced relaxation (37).

It would be of interest to determine whether AHR is associated with airway inflammation and remodeling in athletes. In this regard, Helenius *et al*. observed that the sputum differential cell counts for eosinophils and neutrophils were significantly higher in a group of swimmers than in control subjects. He attributed this increase of inflammatory cells among swimmers to the long-term exposure to chlorine derivatives (7). In bronchoalveolar lavage of healthy subjects, Larsson *et al*. found an increase in the number of granulocytes and macrophages after running in cold air (38). There is a need to further evaluate the presence of airway inflammatory and structural changes in different categories of athletes, particularly in those with AHR.

The presence of subjects with asymptomatic AHR has already been documented among the general population (27,28). At least 20–30% of the subjects with AHR do not report respiratory symptoms compatible with asthma (27,39). In some subjects this may be a preliminary stage to the development of asthma; it has in fact been associated with airway remodeling and inflammation, as in asthma, but to a lesser degree (40).

Furthermore, perception of respiratory symptoms varies considerably from one subject to another, as some individuals are poor perceivers of bronchoconstriction (41–43). This could certainly apply to athletes as well, considering the possible tolerance to nociceptive stimuli, or temporal adaptation to such symptoms when performing intense physical exercise. We have previously proposed that subjects doing regular intense exercise may develop a tolerance to respiratory symptoms (44). This could partly explain the discrepancy observed in athletes between self-reported or physician-diagnosed asthma and the actual presence of AHR or EIB. However, given the extreme stimuli of drying and cooling of the airways following intense increase in minute ventilation during training, it is surprising to observe so few reported manifestations in athletes with abnormal airway function.

It is possible that certain types of sports or training environments could influence the perception of airflow obstruction, as we already observed that swimmers tended to report less breathlessness upon exercise than athletes training in a cold- or dry-air environment (44). Based on our previous report (2), in athletes training mostly in warm/dry-air (such as long-distance runners) and in those training in cold-air (such as cross-country skiers and speed-skaters), the difference between the prevalence of subjective and objective assessment was less pronounced than in triathletes and swimmers. It is difficult to account for the wide discrepancy between prevalences obtained from subjective and objective means in athletes training in indoor pools. It may be related to the fact that high-intensity training in this particular type of environment (pools) makes it difficult to perceive wheezing, breathlessness or phlegm production. It could also be hypothesized that regular exposure to low doses of chlorine could alter airway sensory nerve endings.

Is asthma under-diagnosed in athletes?

The high prevalence of AHR observed in athletes could also suggest that asthma is underdiagnosed when questionnaires are used, as they rely on self-report of symptoms that could be ignored or not well perceived by athletes. This phenomenon of underrecognition of asthma can also exist even with a physician-made diagnosis of asthma, as non-specialist physicians rely primarily on respiratory symptoms or treatment trials to make the diagnosis of asthma (45).

CONCLUSION

One of the difficulties of this analysis is that most studies on physician-diagnosed asthma (Table 1) have used a single study group composed of mixed sports disciplines. Consequently, it has not been possible to verify the variations in prevalence of physician-diagnosed asthma within specific disciplines.

The significance of the high prevalence of AHR in athletes and its effects on performance are uncertain. Increasing efforts should be made to better evaluate the long-term consequences of such features. We believe that athletes should be educated on the possibility of developing asthma, as a large number of them are unaware that they are affected by the condition. Furthermore, to adequately assess airway function in athletes, particularly in regard to the potential risk of developing symptomatic asthma, objective methods are preferable. A heavier reliance on such methods could lead to a better identification of airway dysfunction in athletes with clinical suspicion of asthma.

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